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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,004	02/12/2001	Bassil I. Dahiyat	A-67229-6/RFT/RMS/RMK	1900

7590 11/17/2003

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EXAMINER

WESSENDORF, TERESA D

ART UNIT

PAPER NUMBER

1639

DATE MAILED: 11/17/2003

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/782,004	DAHIYAT ET AL.	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 29 July 2003.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 12-30 is/are pending in the application.
 - 4a) Of the above claim(s) 14-20 and 26-30 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 12,13 and 21-25 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 - a) The translation of the foreign language provisional application has been received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) Interview Summary (PTO-413) Paper No(s) _____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I claims 12-13 and 21-25 in Paper No. 23 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 14-20 and 26-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 23.

Applicants' election of the species of synthesis of secondary library is noted. Applicants state that the elected species reads on claims 21-25 of Group I.

Status of Claims

Claims 12-30 are pending in the application.

Claims 14-20 and 26-30 are withdrawn from consideration as being drawn to non-elected invention.

Claims 12-13 and 21-25 are under examination.

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Specification

The objections to the disclosure have been obviated in view of the amendments to the specification and in part because of applicants' argument.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-13 and 21-25, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The as-filed specification fails to describe a method step of "receiving a library of primary sequences generated utilizing a force filed calculation" i.e., newly added claim step a. Applicants' remarks or as-filed specification does not describe how a library of primary sequences can be received or the means

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or steps of receiving. Furthermore, this step in the context of the as-filed steps does not appear to be in consonant with steps b and c. MPEP 714.02 states that applicant should specifically point out the support for any amendments made to the disclosure.

Claims 12-13 and 21-25, as amended, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzymes protein design using specific program design, does not reasonably provide enablement for any type of secondary library of scaffold protein variants or sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons advanced in the last Office action.

Response to Arguments

Applicants argue that a patent need not teach and preferably omits what is well known in the art. Applicants point the examiner's attention at page 8, lines 13-21 of the specification that discusses secondary library of scaffold protein. Page 14, line 23 up to page 15, line 14 is argued to provide a disclosure of using a force field or alignment program.

In response, applicants fail to recite that which is known in the art that need not be taught in the instant specification. A review of the relied upon section, page 8, lines 13-21 provides for statement as general as the claimed invention. It recites that a scaffold protein may be any protein for which a 3D structure is known or can be generated. **Generally** this can be determined using X-ray crystallography techniques, etc. The scaffold proteins may be from any organisms. To generate a scaffold for a single, let alone, for a library of any organisms from the various broad lists of techniques, coupled with the broad claimed steps of calculation and generation of probability distribution table of amino acid residues would be undue experimentation. Applicants recite too numerous general statements lacking any specifics. Similarly page 14 recited computational methods using SCMF. The claims do not recite for any computation methods and unclear as to how the primary sequences is received by force field calculation. Thus, the separate and discrete sections rely upon does not provide for a scope of the enabling disclosure as claimed. Applicants cite *In re Goffe*, 191 USPQ 429 (CCPA 1976).

In response, applicants are working in a field of biochemistry where little prediction is possible and that the scope of claims should not be unduly extensive in such fields

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where applicability is highly speculative or not explored. Applicants may not preempt an unduly large field by the expedient of making broad prophetic statements in the specification and claims unless the accuracy of such statements is sufficiently supported by well established chemical principles or by sufficient number of examples.

Applicant cites *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976) for the proposition that applicant is not required to test every species covered by the broad claim.

In reply, there is not an instance where applicant has been required to test every species. Rather, applicants have not provided a reasonable assurance that the species covered by the broad scope of the claims will correspond or meet the objective of the claimed invention. This is especially true since *the single working example, supposedly a guide to the practice of the broad claimed invention, does not use a force field calculation. As a skilled in the art appreciates, to date there are too numerous obstacles for the design of even a single secondary structure of a protein, let alone, all or any kinds of proteins. For example, the combinatorial large number of possible sequences and the incomplete understanding of the factors that control protein structure are still the primary obstacles in protein design. The Examples clearly illustrate the*

need to impose restrictions for the successful design of the secondary structure of the enzyme protein. Amino acid residues are selected such that cys is not used to prevent disulfide formation or Gly that can compromise flexibility and Pro for which an appropriate rotamer is difficult to define. Note further the restriction in the computer design using known primary structure of the known enzyme as obtained from the Protein Data Bank wherein water and SO2 have been deleted to remove any obstacles for its successful design. Therefore, the broad claimed method drawn to any type of protein simply utilizing the force field calculation that results in a secondary structure for any or all type of proteins requires an undue amount of experimentation.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-13 and 21-25, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

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which applicant regards as the invention for reasons advanced in the last Office action.

Response to Arguments

A). Applicants argue that force field calculations may be used to create a probability distribution table based on the results of the calculations.

In reply, this is contrary to what is being claimed i.e., step a) of claim 12 where the force field calculations is used to receive a primary sequences.

It is argued that the results of a force field calculation or other computational method may be analyzed in a probability distribution table.

In response, such calculation and probability distribution table would only be feasible with the aid of a computer. Since probability distribution of variants would include an enormous amount of data that can only be handled by a computer. To do otherwise, as the claims recite, would be indefinite lacking the essential step (computer step) to enable such determination.

Newly amended claim 12 which recites sequence in the preamble appears inconsistent with step b) of the body of the claims which recites for a "plurality of variant positions" from said primary sequences. It is not clear as to which positions from said primary sequences are considered variants thereof.

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The rejection as to the used of the term "probability" in the last Office action has not been responded thereto by applicants. Since applicants have not responded to this rejection, it is believed that applicants are acquiescing therewith.

B). The rejection of the claim under this paragraph has been obviated with the amendment to the claims.

The rejections under paragraphs C-E are moot since these are non-elected claims.

F). Claims 21-25 are rejected for the same reasons set forth in the last Office action.

Response to Arguments

Applicants argue that claim 25 has been canceled, therefore the rejection with respect to this claim is moot. Applicants argue that claims 21-23 are directed to synthesizing the protein sequences of the preceding claims. And refer to relevant sections in the specification. Applicants argue that "equimolar" is a term of art.

In response, the REMARKS of 7/20/03 recites that claim 25 has not been cancelled. The rejection of claim 25 is therefore maintained. Likewise, applicants' arguments with respect to claims 21-23 are unclear. It is not clear as to how the proteins are synthesized from an oligonucleotide when the base claim

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recites generating proteins not oligonucleotides. With respect to the terms "relative" amounts (claim 25) and "equimolar amounts" being indefinite, it is not the definitions that is at issue. Rather, the e.g., amount in the context of the claim that is considered e.g., equimolar or relative.

Double Patenting

The obviousness double patenting rejection of claims 16-20 are rejected over claims 1,22 of U.S. Patent No. 6,269,312 ([312 Patent (1)] or claims 1-8 of U.S. Patent No. 6,403,312 ['312(11)] is moot as these claims are non-elected. However, if applicants decide to prosecute these claims in later applications, then the rejection will be revived.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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Claims 12-13 and 21-25, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayo in view of applicants' disclosure of known prior art for reasons set forth in the last Office action.

Response to Arguments

Applicants argue that there is no suggestion or teaching of generating a secondary library from secondary sequences different from the primary sequences.

In response, attention is directed to page 7, line 23 up to page 11, line 26 and claim 1, page 80 of the Mayo reference. Thus, the rotamers, which are group of amino acids that can be used in variant positions of a template are used to obtain an optimized peptide (i.e., the secondary library as claimed). Accordingly, Mayo discloses a similar method as claimed except perhaps, in the terminologies coined by applicants.

Applicants argue that "DNA shuffling" and other well-known mutagenesis techniques, teach away from the use of a rational computational design algorithm, as used in the instant application.

In response, applicants cannot read limitations set forth in the specification into the claims. The claims do not recite for a computational design algorithm. As stated above, the concept of producing a secondary library is similarly disclosed

by Mayo which teaches optimized sequences obtained from a primary or template backbone sequence. A force field calculation is similarly taught by Mayo. The probability distribution as claimed is taught by Mayo when set of rotamers is used to replace variable positions in the template backbone (primary sequences as claimed) sequences. Applicants' disclosure that synthesis is known in the art for a known sequences would suggest to one having ordinary skill in the art that the optimized sequences of Mayo can be synthesized. One having ordinary skill in the art would be motivated to sequence the optimized sequences obtained by Mayo in order to correctly identified the sequences that are contained in the library and the optimized sequences, specifically.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this

action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 14-20 and 26-30 drawn to an invention nonelected without traverse. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned

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are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T.D.W.
T. D. Wessendorf
Primary Examiner
Art Unit 1627

tdw

November 14, 2003